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**AMENDMENTS**

1-43. (cancelled)

44. (currently amended) An agent for inhibiting at least one of release, maturation and replication of a member of the Flaviviridae family selected from Flavivirus, or Pestivirus ~~and Hepacivirus~~ wherein the agent comprises, as an active component, at least one proteasome inhibitor in a pharmaceutical preparation.

45. (currently amended) An agent as claimed in claim 44, wherein the agent ~~inhibits at least one of release, maturation and replication of hepatitis C virus (HCV)~~ and is used for the treatment and prophylaxis of HCV-induced hepatitides, flavivirus-induced fever, hemorrhages, leukopenia, thrombocytopenia, diarrheal diseases, and encephalitides ~~and also or~~ pestivirus-induced diseases.

46. (previously presented) An agent as claimed in claim 45, wherein the proteasome inhibitor is a substance which inhibits, regulates or otherwise affects the activities of the ubiquitin/proteasome pathway; which specifically affects the enzymic activities of the complete 26S proteasome complex; and which specifically affects the enzymic activities of the free 20S, catalytically active, proteasome complex, which is not assembled with regulatory subunits.

47. (previously presented) An agent as claimed in claim 45, wherein the proteasome inhibitor is taken up by higher eukaryotic cells and, after having been taken up into a cell, interacts with the catalytic subunits of the proteasome, and, in connection with this, blocks at least some of the proteolytic activities of the proteasome within the 26S or the 20S proteasome complex.

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48. (previously presented) An agent as claimed in claim 45, wherein in addition to proteasome inhibitors, the pharmaceutical preparation also comprises at least one further agent which affects, regulates or inhibits the cellular ubiquitin system, such as the activities of the ubiquitin-conjugating enzymes and/or of the ubiquitin-hydrolyzing enzymes.

49. (previously presented) An agent as claimed in claim 45, wherein the proteasome inhibitor is administered in various forms *in vivo*, i.e. orally, intravenously, intramuscularly, subcutaneously or in encapsulated form, with or without cell specificity-carrying changes, which, due to using a particular administration and/or dose regime, exhibit low cytotoxicity, which do not elicit any side effects, or only elicit insignificant side effects, and which exhibit a relatively high metabolic half life and a relatively low clearance rate in the body.

50. (previously presented) An agent as claimed in claim 45, wherein the proteasome inhibitor

- a) is isolated in natural form from microorganisms or other natural sources; or
- b) is formed from natural substances as a result of chemical modifications; or
- c) is prepared completely synthetically; or
- d) is synthesized *in vivo* using gene therapy methods.

51. (previously presented) An agent as claimed in claim 50, wherein the proteasome inhibitor belongs to the following substance classes:

- a) naturally occurring proteasome inhibitors:
  - peptide derivatives which contain epoxyketone structures C-terminally,

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- $\beta$ -lactone derivatives,
  - aclacinomycin A (also termed aclarubicin),
  - lactacystin and its chemically modified variants, such as the cell membrane-penetrating variant "clastolactacystein  $\beta$ -lactone"
- b) synthetically prepared proteasome inhibitors:
- modified peptide aldehydes, such as N-carbobenzoxymethyl-L-leucyl-L-leucyl-L-leucinal (also designated MG132 or ZLLL), its boric acid derivative MG232; N-carbobenzoxymethyl-Leu-Leu-Nva-H (designated MG115; N-acetyl-L-leucyl-L-leucyl-L-norleucinal (designated LLnL) and N-carbobenzoxymethyl-Ile-Glu(OBzl)-Ala-Leu-H (also designated PSI);
- c) peptides which carry an  $\alpha,\beta$ -epoxy ketone structure C-terminally, and also vinylsulfones, such as carbobenzoxymethyl-L-leucyl-L-leucyl-L-leucinevinylsulfone, or 4-hydroxy-5-iodo-3-nitrophenylacetyl-L-leucyl-L-leucyl-L-leucinevinylsulfone (NLVS)
- d) glyoxylic acid or boric acid radicals, such as pyrazyl-CONH(CHPh)CONH(CHisobutyl)B(OH)<sub>2</sub> and also dipeptidyl boric acid derivatives, or
- e) pinacol esters, such as benzyloxycarbonyl(Cbz)-Leu-Leu-boroLeu pinacol ester.

52. (previously presented) An agent as claimed in claim 50 wherein the particularly suitable proteasome inhibitor is the epoxyketone epoxomicin (epoxomicin, molecular formula: C<sub>28</sub>H<sub>36</sub>N<sub>4</sub>O<sub>7</sub>) and/or eponemicin (eponemicin, molecular formula: C<sub>20</sub>H<sub>36</sub>N<sub>2</sub>O<sub>5</sub>).

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53. (previously presented) An agent as claimed in claim 50 wherein the particularly suitable proteasome inhibitor is selected from the PS series

- a) PS-519 as  $\beta$ -lactone, and also as lactacystin derivative the compound IR-[1S,4R,5S]-1-(1-hydroxy-2-methylpropyl)-4-propyl-6-oxa-2-azabicyclo[3.2.0]heptane-3,7-dione - molecular formula  $C_{12}H_{19}NO_4$  - and/or
- b) PS-341 as peptidyl-boric acid derivative the compound N-pyrazinecarbonyl-L-phenylalanine-L-leucine-boric acid - molecular formula  $C_{19}H_{25}BN_4O_4$  - and/or
- c) PS-273 (morpholine-CONH-(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>) and its enantiomer PS-293 and/or
- d) compound PS-296 (8-quinolylsulfonyl-CONH-(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>) and/or
- e) PS-303 (NH<sub>2</sub>(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>) and/or
- f) PS-321 as (morpholine-CONH-(CH-naphthyl)-CONH-(CH-phenylalanine)-B(OH)<sub>2</sub>); - and/or
- g) PS-334 (CH<sub>3</sub>-NH-(CH-naphthyl)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>) and/or
- h) the compound PS-325 (2-quinol-CONH-(CH-*homo*-phenylalanine)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>) and/or
- i) PS-352 (phenylalanine-CH<sub>2</sub>-CH<sub>2</sub>-CONH-(CH-phenylalanine)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>) and/or
- j) PS-383 (pyridyl-CONH-(CH-*pF*-phenylalanine)-CONH-(CH-isobutyl)-B(OH)<sub>2</sub>).

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54. (currently amended) ~~The use of proteasome inhibitors as claimed in claim 44 for~~ A method of inhibiting at least one of the entry/internalization process, the replication and the maturation and release of Flaviviridae with the agent of claim 44.

55. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54, wherein the proteasome inhibitor inhibits ~~for inhibiting~~ late processes in the Flaviviridae life cycle.

56. (currently amended) ~~The use as claimed in~~ The method of claim 54, wherein the proteasome inhibitor at least effectively blocks to a large extent or completely prevent the production of infectious virions from Flaviviridae-infected cells.

57. (currently amended) ~~The use as claimed in~~ The method of claim 54, wherein the proteasome inhibitor causes inhibition of the release of virions and also reduces the infectivity of the virions which are released.

58. (currently amended) ~~The use as claimed in~~ The method of claim 54, wherein the proteasome inhibitor suppresses virus replication and thus the spread of an infection in vivo, ~~i.e. in the liver tissue of an infected patient in the case of hepatitis C virus.~~

59. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54, wherein the proteasome inhibitor inhibits ~~for inhibiting~~ the replication of Flaviviridae in accordance with the following mechanisms

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- a) blocking/reducing the release of new virions;
- b) blocking/reducing the infectivity of released virions;
- c) blocking/reducing the spread of infection in cultures of host cells;
- d) blocking/reducing the spread of infection in infected organs *in vivo*.

60. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54,  
wherein the proteasome inhibitor suppresses for suppressing flavivirus infections and pestivirus  
infections in humans and animals.

61. (previously presented) The use of proteasome inhibitors as claimed in claim 54 for inducing  
the death of hepatocarcinoma cells.

62. (previously presented) The use of proteasome inhibitors as claimed in claim 61 for  
suppressing and/or preventing the development of liver cell carcinomas.

63. (previously presented) The use of proteasome inhibitors as claimed in claim 62 for treating  
patients who have established liver cell carcinomas.

64. (previously presented) The use of proteasome inhibitors as claimed in claim 61 for  
treating/controlling/preventing HCV-induced liver cirrhosis and/or HCV-induced liver cell  
carcinomas, medicament-induced liver carcinomas, genetically determined liver carcinomas,  
environmentally determined liver carcinomas and/or liver carcinomas which are determined by a  
combination of viral and nonviral factors.

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65. (previously presented) The use of proteasome inhibitors as claimed in claim 61 for selectively eliminating liver carcinoma cells which develop as the result of a HCV infection, or a corresponding coinfection with HCV and hepatitis B virus (HBV), or a hepatitis delta virus (HDV)/HBV/HCV coinfection, human immunodeficiency virus (HIV)/HCV coinfections, or HCV and coinfections with other viruses, bacteria or parasites.

66. (previously presented) The use of proteasome inhibitors as claimed in claim 61 for preventing the development, growth and metastasis of liver cell tumors and for preferentially destroying liver carcinoma cells in HCV-infected patients.

67. (previously presented) The use of proteasome inhibitors as claimed in claim 54 for modulating the expression, modification and activity of the tumor suppressor protein p53 and other tumor suppressor proteins which are of importance in connection with hepatocellular carcinomas (HCCs).

68. (previously presented) The use of proteasome inhibitors as claimed in claim 54 for liver cell regeneration in patients suffering from hepatitis.

69. (previously presented) The use of proteasome inhibitors as claimed in claim 54 for regenerating patients following flavivirus infections.

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70. (previously presented) The use of proteasome inhibitors as claimed in claim 54 for regenerating stabled animals following flavivirus or pestivirus infections.

71. (previously presented) The use of proteasome inhibitors as claimed in claim 54 for reducing the number of infected virus-producing cells in liver cell tissue.

72. (currently amended) ~~The use as claimed in~~ The method of claim 54, wherein the proteasome ~~inhibitors alter~~ inhibitor alters the post-translational modification and proteolytic processing of Flaviviridae structural proteins and reduce the ability of the virus envelope proteins to dimerize and thereby reduce or block the release and infectivity of Flaviviridae.

73. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54, ~~wherein the proteasome inhibitor inhibits for inhibiting~~ both the maintenance and persistence of a previously established infection and of a secondary infection including blocking the spread of a Flaviviridae infection in vivo.

74. (currently amended) ~~The use of more than one proteasome inhibitor as claimed in claim 50 in combination for the purpose~~ A method of treating and controlling HCV-induced hepatitis, flavivirus-induced fever, hemorrhages and encephalitides and pestivirus-induced diseases with the agent of claim 50, wherein the agent comprises a combination of proteasome inhibitors.



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75. (currently amended) ~~The use as claimed in~~ The method of claim 74, wherein the combination further comprises in combination with therapeutic agents which are already used in the antiviral therapy of Flaviviridae infections.

76. (currently amended) ~~The use as claimed in~~ The method of claim 74, wherein the combination is administered to treat for treating coinfections with different flaviviruses and pestiviruses.

77. (currently amended) ~~The use as claimed in~~ The method of claim 74, wherein the combination is administered to treat for treating coinfections of HCV and immunodeficiency viruses HIV-1 and HIV-2.

78. (currently amended) ~~The use as claimed in~~ The method of claim 77, wherein the combination is administered to treat for treating HCV/HIV coinfections in combination with HAART therapy.

79. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54, wherein the proteasome inhibitor prevents for preventing a reinfection with HCV in connection with liver transplantations and other organ transplantations.

80. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54, wherein the proteasome inhibitor prevents for preventing a reinfection with HCV in connection with cell therapies, by means of administering the agents before, during and after the transplantation.

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81. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54,  
wherein the proteasome inhibitor prevents ~~for preventing~~ a reinfection with HCV in connection  
with the transplantation of virus-free organs to chronic virus carriers who still possess residual  
virus and can infect new organs and also in connection with the transfer of virus-containing  
organs from donors to virus-free patients.

82. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54,  
wherein the proteasome inhibitor prevents ~~for preventing~~ the establishment of a systemic  
Flaviviridae infection immediately following contact with infectious virus.

83. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54,  
wherein the proteasome prevents ~~for preventing~~ a Flaviviridae infection in individuals who are at  
a high risk of fresh infection.

84. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 54,  
wherein the proteasome decreases or eliminates ~~for decreasing or eliminating~~ a hepatitis by  
means of immune system-mediated mechanisms.

85. (currently amended) ~~The use of proteasome inhibitors as claimed in claim 50 for~~ A method  
of producing agents and/or pharmaceutical preparations for inhibiting the release, maturation and  
replication of Flaviviridae with at least one proteasome inhibitor, wherein the agent is the agent  
of Claim 50.

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86. (currently amended) ~~The use of proteasome inhibitors as claimed in~~ The method of claim 85,  
wherein the agent comprises at least one proteasome inhibitor for producing pharmaceuticals for  
the treatment and prophylaxis of HCV-induced hepatitides, flavivirus-induced fever,  
hemorrhages and encephalitides and pestivirus-induced diseases.